

## P, ENT COOPERATION TREA.

From the INTERNATIONAL BUREAU

PCT

**NOTIFICATION OF ELECTION**  
 (PCT Rule 61.2)

To:

Assistant Commissioner for Patents  
 United States Patent and Trademark  
 Office  
 Box PCT  
 Washington, D.C.20231  
 ETATS-UNIS D'AMERIQUE

<b>Date of mailing (day/month/year)</b>
16 May 2000 (16.05.00)

in its capacity as elected Office

<b>International application No.</b>
PCT/GB99/03286

**Applicant's or agent's file reference**  
 PG3565/PCT

<b>International filing date (day/month/year)</b>
05 October 1999 (05.10.99)

**Priority date (day/month/year)**  
 05 October 1998 (05.10.98)

<b>Applicant</b>
CARR, Robin, Arthur, Ellis et al

1. The designated Office is hereby notified of its election made:

in the demand filed with the International Preliminary Examining Authority on:

17 April 2000 (17.04.00)

in a notice effecting later election filed with the International Bureau on:

\_\_\_\_\_

2. The election  was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Juan Cruz Telephone No.: (41-22) 338.83.38
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# PATENT COOPERATION TREATY

in the INTERNATIONAL SEARCHING AUTHORITY

**PCT**

To:

GLAXO WELLCOME PLC  
Glaxo Wellcome House  
Attn. Quillin, Helen K.  
Berkeley Avenue  
Greenford  
Middlesex UB6 0NN  
UNITED KINGDOM

Global Information Network	THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION
RECEIVED	(PCT Rule 44.1)
31 JUL 2000	
SM	Date of mailing (day/month/year)
	28/07/2000

NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL SEARCH REPORT  
OR THE DECLARATION

(PCT Rule 44.1)

Applicant's or agent's file reference <b>PG3565/PCT</b>	<b>FOR FURTHER ACTION</b> See paragraphs 1 and 4 below.
International application No. <b>PCT/GB 99/ 03286</b>	International filing date (day/month/year) <b>05/10/1999</b>
Applicant <b>GLAXO GROUP LIMITED et al.</b>	

1.  The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

**Filing of amendments and statement under Article 19:**

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

**When?** The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

**Where?** Directly to the International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland  
Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2.  The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3.  **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority  European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer <b>John De Bruijn</b>
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## **NOTE TO FORM PCT/ISA/220**

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

### **INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19**

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

#### **What parts of the International application may be amended?**

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

#### **When?**

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

#### **Where not to file the amendments?**

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been filed, see below.

#### **How?**

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

**The amendments must be made in the language in which the International application is to be published.**

#### **What documents must/may accompany the amendments?**

##### **Letter (Section 205(b)):**

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

**The letter must be in English or French, at the choice of the applicant. However, if the language of the International application is English, the letter must be in English; if the language of the International application is French, the letter must be in French.**

## NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

**The following examples illustrate the manner in which amendments must be explained in the accompanying letter:**

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:  
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:  
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:  
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or  
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:  
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

### "Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

**It must be in the language in which the international application is to be published.**

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

### Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

### Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

\*For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

PG3565/PCT

PCT/GB 99/ 03286

05/10/1999

05/10/1998

GLAXO GROUP LIMITED et al.

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X

X

X

X

IPC 7 C07B61/00 C07D239/38 C07C271/20 C07C311/18 C07C237/18

IPC 7 C07B

EPO-Internal, WPI Data, PAJ

A CARRASCO M R ET AL: "Direct Monitoring of  
Organic Reactions on Polymeric Supports"  
TETRAHEDRON LETTERS, NL, ELSEVIER SCIENCE  
PUBLISHERS, AMSTERDAM,  
vol. 38, no. 36,  
8 September 1997 (1997-09-08), pages  
6331-6334, XP004087929  
ISSN: 0040-4039  
cited in the application  
page 6331  
scheme 1  
figure 1

1,42-49

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X

X

18 July 2000

28/07/2000

1

Held, P

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 99/03286

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>GEYSEN H M ET AL: "ISOTOPE OR MASS ENCODING OF COMBINATORIAL LIBRARIES" CHEMISTRY AND BIOLOGY, GB, CURRENT BIOLOGY, LONDON, vol. 3, no. 8, 1 August 1996 (1996-08-01), pages 679-688, XP002035873 ISSN: 1074-5521 cited in the application page 679, right-hand column, last paragraph -page 680, left-hand column, paragraph 1 page 686, left-hand column, last paragraph figure 1</p> <p>---</p> <p>WO 97 37953 A (GLAXO GROUP LTD ;GEYSEN HENDRIK M (US); KINDER DANIEL START (US);) 16 October 1997 (1997-10-16) cited in the application page 10, line 21 -page 12, line 13 figures 13-17</p> <p>---</p> <p>WO 95 28640 A (UNIV COLUMBIA ;COLD SPRING HARBOR LAB (US); STILL W CLARK (US); WI) 26 October 1995 (1995-10-26) claims 1,38</p> <p>-----</p>	1,42-49
A		1,42-48
A		1,42-48

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International Application No

PCT/GB 99/03286

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO 9737953 A	16-10-1997	AU	2723797 A	29-10-1997
		CA	2242171 A	16-10-1997
		CZ	9802176 A	16-12-1998
		EP	0863858 A	16-09-1998
		HU	9901560 A	30-08-1999
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WO 9528640 A	26-10-1995	US	5565324 A	15-10-1996
		AU	2292695 A	10-11-1995
		CA	2187792 A	26-10-1995
		CN	1151793 A	11-06-1997
		EP	0755514 A	29-01-1997
		HU	74985 A	28-03-1997
		JP	10502614 T	10-03-1998
		NO	964332 A	03-12-1996
		US	5968736 A	19-10-1999
		US	6001579 A	14-12-1999
		US	5789172 A	04-08-1998
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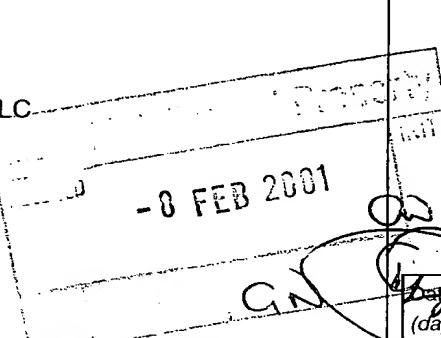
# PATENT COOPERATION TREATY

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

**PCT**

NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT

(PCT Rule 71.1)

<p>To:</p> <p>Quillin, Helen K. GLAXO WELLCOME PLC Glaxo Wellcome House Berkeley Avenue Greenford Middlesex UB6 0NN GRANDE BRETAGNE</p>	 <p>Date of mailing (day/month/year) <b>106.02.01</b></p>	
<p>Applicant's or agent's file reference <b>PG3565/PCT</b></p> <p><b>IMPORTANT NOTIFICATION</b></p>		
International application No. <b>PCT/GB99/03286</b>	International filing date (day/month/year) <b>05/10/1999</b>	Priority date (day/month/year) <b>05/10/1998</b>
<p>Applicant <b>GLAXO GROUP LIMITED et al.</b></p>		

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

**4. REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/ <hr/> European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Roche, S  Tel.+49 89 2399-8031
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## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PG3565/PCT	<b>FOR FURTHER ACTION</b>		See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/GB99/03286	International filing date (day/month/year) 05/10/1999	Priority date (day/month/year) 05/10/1998	
International Patent Classification (IPC) or national classification and IPC C07B61/00			
Applicant GLAXO GROUP LIMITED et al.			

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of .5 sheets, including this cover sheet.
  - This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 1 sheets.

3. This report contains indications relating to the following items:

- I    Basis of the report
- II    Priority
- III    Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV    Lack of unity of invention
- V    Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI    Certain documents cited
- VII    Certain defects in the international application
- VIII    Certain observations on the international application

Date of submission of the demand 17/04/2000	Date of completion of this report 06.02.01
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer  Kleidernigg, O  Telephone No. +49 89 2399 2143



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/GB99/03286

**I. Basis of the report**

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).)*:

**Description, pages:**

1-82                   as originally filed

**Claims, No.:**

8-49                   as originally filed

1-7                   with telefax of                   30/11/2000

**Drawings, sheets:**

1/18-18/18           as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/GB99/03286

the description,      pages:  
 the claims,           Nos.:  
 the drawings,        sheets:

5.  This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes:	Claims 1-45,48,49
	No:	Claims 46,47
Inventive step (IS)	Yes:	Claims 1-45,48,49
	No:	Claims 46,47
Industrial applicability (IA)	Yes:	Claims 1-49
	No:	Claims

2. Citations and explanations  
see separate sheet

**VII. Certain defects in the international application**

The following defects in the form or contents of the international application have been noted:  
see separate sheet

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB99/03286

**ad Section V**

**Novelty & Inventive step**

The present application is directed to a chemical construct (claims 1-41) for use in solid phase synthesis comprising a solid support Q having linked thereto via a connecting group Y a substrate R; the connecting group Y having first and second cleavage sites which are orthogonally and selectively cleavable; the second cleavage site being selectively cleavable to release the substrate; and the first cleavage site being located at a position between the second cleavage site and the solid support and being selectively cleavable to release a fragment Fr comprising the substrate and at least a portion of the connecting group Y; characterized in that cleavage of the skeleton of the construct at the first cleavage site forms or introduces on the chemical fragment Fr at the first cleavage site a moiety comprising a sensitising group G which sensitises the chemical fragment Fr to instrumental, e.g. mass spectroscopic, analysis, methods for analysing the constructs (claims 42, 46-49) and intermediates (claims 43-45).

TETRAHEDRON LETT., vol. 38, no. 36, 1997, p. 6331-6334 (D1) represents the closest prior art and differs from the subject matter of the present application insofar that group necessary to ionize and sensitize the chemical fragment is already present before cleavage of the first cleavage site (cf. page 6332, scheme 1).

Thus, the subject matter of claims 1-45, 48, 49 is fulfilling the criteria of Article 33(2) PCT.

The technical problem may regarded as the provision of improved means for monitoring chemical reactions on solid supports.

The solution given in claim 1 relates to chemical constructs in which a sensitising group is induced upon cleavage. Starting from D1, which discloses that the sensitising group is present in the construct before cleavage, the solution proposed in the present application is not directly deducible for a person skilled in the art from D1.

Thus, the subject matter of present claims 1-45, 48, 49 is fulfilling the requirements of Article 33(3) PCT.

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB99/03286

However, method claims 46 and 47 concerning the UV-VIS or FLU spectrophotometric analysis are not limited to chemical constructs in which a sensitising group is induced upon cleavage. Thus, the latter claims are neither novel nor inventive over the prior art of D1.

**ad Section VII**

The passage on page 82 , lines 7-11 is not fulfilling the criteria of Rule 9.1 iv) PCT and should accordingly be deleted.

Claim 43 is unclear (Article 6 PCT), because the group Q' is not present in the formula representing the intermediate construct.

30-11-2000

PG3563-PCT

GB 009903286

November 2000.

CLAIMS

1. A chemical construct for use in solid phase synthesis comprising a solid support Q having linked thereto via a connecting group Y a substrate R; the connecting group Y having first and second cleavage sites which are orthogonally and selectively cleavable; the second cleavage site being selectively cleavable to release the substrate; and the first cleavage site being located at a position between the second cleavage site and the solid support and being selectively cleavable to release a fragment Fr comprising the substrate and at least a portion of the connecting group Y; characterised in that cleavage of the skeleton of the construct at the first cleavage site forms or introduces on the chemical fragment Fr at the first cleavage site a moiety comprising a sensitising group G which sensitises the chemical fragment Fr to instrumental, e.g. mass spectroscopic, analysis.  
5
2. A chemical construct according to claim 1 wherein the chemical fragment Fr contains a means for imparting a characteristic signature to the mass spectrum of the fragment.  
10
3. A chemical construct according to claim 2 wherein the characteristic signature is provided by incorporating into the fragment Fr a peak splitting isotopic label.  
15
4. A chemical construct according to claim 3 wherein the peak splitting isotopic label is defined one or more isotope pairs selected from  $^1\text{H}/^2\text{D}$ ,  $^{79}\text{Br}/^{81}\text{Br}$ ,  $^{12}\text{C}/^{13}\text{C}$ ,  $^{14}\text{N}/^{15}\text{N}$  and  $^{16}\text{O}/^{18}\text{O}$ .  
20
5. A chemical construct according to any one of claims 2 to 4 wherein the means for imparting a characteristic signature to the mass spectrum of the fragment is located between the first and second cleavage sites.  
25
6. A chemical construct according to any one of the preceding claims wherein the first and second cleavage sites are defined by first and second linker groups  $\text{L}^1$  and  $\text{L}^2$ .  
30
7. A chemical construct according to claim 6 wherein an spacer group A is interposed between the two linker groups  $\text{L}^1$  and  $\text{L}^2$ , the spacer group A containing means for imparting a characteristic signature to the mass spectrum of the fragment Fr as defined in any one of claims 2 to 5.

## INTERNATIONAL COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>PG3565/PCT</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/GB 99/ 03286</b>	International filing date ( <i>day/month/year</i> ) <b>05/10/1999</b>	(Earliest) Priority Date ( <i>day/month/year</i> ) <b>05/10/1998</b>
Applicant <b>GLAXO GROUP LIMITED et al.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
  - the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing :
  - contained in the international application in written form.
  - filed together with the international application in computer readable form.
  - furnished subsequently to this Authority in written form.
  - furnished subsequently to this Authority in computer readable form.
  - the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
  - the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2.  Certain claims were found unsearchable (See Box I).

3.  Unity of Invention is lacking (see Box II).

4. With regard to the title,

- the text is approved as submitted by the applicant.
- the text has been established by this Authority to read as follows:

5. With regard to the abstract,

- the text is approved as submitted by the applicant.
- the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

- as suggested by the applicant.
- because the applicant failed to suggest a figure.
- because this figure better characterizes the invention.

None of the figures.

**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification <sup>7</sup> : <b>C07B 61/00, C07D 239/38, C07C 271/20, 311/18, 237/18</b>	A3	(11) International Publication Number: <b>WO 00/20357</b> (43) International Publication Date: <b>13 April 2000 (13.04.00)</b>
(21) International Application Number: <b>PCT/GB99/03286</b>		
(22) International Filing Date: <b>5 October 1999 (05.10.99)</b>		
(30) Priority Data: <b>9821655.9 5 October 1998 (05.10.98) GB</b>		
(71) Applicant (for all designated States except US): <b>GLAXO GROUP LIMITED [GB/GB]; Glaxo Wellcome House, Berkeley Avenue, Greenford, Middlesex UB6 0NN (GB).</b>		CINSKI, Jan, Josef [GB/GB]; Glaxo Wellcome Chemistry Laboratory, University Chemistry Laboratories, The University of Cambridge, Lensfield Road, Cambridge CB2 1EW (GB). WATSON, Stephen, Paul [GB/GB]; Glaxo Wellcome plc, Gunnels Wood Road, Stevenage, Hertfordshire SG1 2NY (GB). WILLIAMS, Geoffrey, Martyn [NZ/GB]; Glaxo Wellcome Chemistry Laboratory, The University of Cambridge, Lensfield Road, Cambridge CB2 1EW (GB). ZARAMELLA, Alessio [IT/IT]; Glaxo Wellcome SpA, Via Alessandro Fleming, 2, I-37100 Verona (IT).
(72) Inventors; and		
(75) Inventors/Applicants (for US only): <b>CARR, Robin, Arthur, Ellis [GB/GB]; Glaxo Wellcome plc, Gunnels Wood Road, Stevenage, Hertfordshire SG1 2NY (GB). GEHANNE, Sylvie [FR/IT]; Glaxo Wellcome SpA, Via Alessandro Fleming, 2, I-37100 Verona (IT). KAY, Corinne [FR/GB]; Glaxo Wellcome Chemistry Laboratory, University Chemistry Laboratories, The University of Cambridge, Lensfield Road, Cambridge CB2 1EW (GB). McKEOWN, Stephen, Carl [GB/GB]; Glaxo Wellcome plc, Gunnels Wood Road, Stevenage, Hertfordshire SG1 2NY (GB). MURRAY, Peter, John [GB/GB]; OSI Pharmaceuticals, Aston Molecules Limited, 10 Holt Court South, Aston Science Park, Birmingham B7 4EJ (GB). PAIO, Alfredo [IT/IT]; Glaxo Wellcome SpA, Via Alessandro Fleming, 2, I-37100 Verona (IT). SCI-</b>		
		(74) Agent: <b>QUILLIN, Helen, K.; Glaxo Wellcome plc, Glaxo Wellcome House, Berkeley Avenue, Greenford, Middlesex UB6 0NN (GB).</b>
		(81) Designated States: <b>AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).</b>
		<b>Published:</b> <i>With international search report.</i>
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(54) Title: CHEMICAL CONSTRUCTS

(57) Abstract

The invention provides a chemical construct for use in solid phase synthesis comprising a solid support Q having linked thereto via a connecting group Y a substrate R; the connecting group Y having first and second cleavage sites which are orthogonally and selectively cleavable; the second cleavage site being selectively cleavable to release the substrate; and the first cleavage site being located at a position between the second cleavage site and the solid support and being selectively cleavable to release a fragment Fr comprising the substrate and at least a portion of the connecting group Y; characterised in that cleavage at the first cleavage site forms or introduces on the chemical fragment Fr at the first cleavage site a moiety comprising a sensitising group G (such as an amino group) which sensitises the chemical fragment Fr to instrumental, e.g. mass spectroscopic, analysis. Also provided are methods of analysis employing the constructs, as well as intermediate constructs.

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# INTERNATIONAL SEARCH REPORT

Int'l. Application No.  
PCT/GB 99/03286

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07B61/00 C07D239/38 C07C271/20 C07C311/18 C07C237/18

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

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## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>CARRASCO M R ET AL: "Direct Monitoring of Organic Reactions on Polymeric Supports"  <b>TETRAHEDRON LETTERS</b>, NL, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM,  vol. 38, no. 36,  8 September 1997 (1997-09-08), pages 6331-6334, XP004087929  ISSN: 0040-4039  cited in the application  page 6331  scheme 1  figure 1</p> <p>---</p> <p style="text-align: center;">-/--</p>	1,42-49

Further documents are listed in the continuation of box C.

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Int'l Search Report  
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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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A	<p>GEYSEN H M ET AL: "ISOTOPE OR MASS ENCODING OF COMBINATORIAL LIBRARIES" CHEMISTRY AND BIOLOGY, GB, CURRENT BIOLOGY, LONDON, vol. 3, no. 8, 1 August 1996 (1996-08-01), pages 679-688, XP002035873 ISSN: 1074-5521 cited in the application page 679, right-hand column, last paragraph -page 680, left-hand column, paragraph 1 page 686, left-hand column, last paragraph figure 1</p> <p>---</p>	1,42-49
A	<p>WO 97 37953 A (GLAXO GROUP LTD ;GEYSEN HENDRIK M (US); KINDER DANIEL START (US);) 16 October 1997 (1997-10-16) cited in the application page 10, line 21 -page 12, line 13 figures 13-17</p> <p>---</p>	1,42-48
A	<p>WO 95 28640 A (UNIV COLUMBIA ;COLD SPRING HARBOR LAB (US); STILL W CLARK (US); WI) 26 October 1995 (1995-10-26) claims 1,38</p> <p>-----</p>	1,42-48

# INTERNATIONAL SEARCH REPORT

Information on patent family members

Int	Application No
	PCT/GB 99/03286

Patent document cited in search report	Publication date	Patent family member(s)			Publication date
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		US 5968736 A			19-10-1999
		US 6001579 A			14-12-1999
		US 5789172 A			04-08-1998

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## REQUEST

The undersigned requests that the present International application be processed according to the Patent Cooperation Treaty

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Chemical Constructs

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Glaxo Group Limited  
Glaxo Wellcome House  
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UB6 0NN, GB

This person is also inventor.

Telephone No. 0171 493 4060

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State (i.e. country) of nationality:

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CARR, Robin Arthur Ellis  
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Gunnels Wood Road  
evenage  
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SG1 2NY, GB

This person is:

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- applicant and inventor
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QUILLIN, Helen K.  
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GEHANNE, Sylvie  
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Via Alessandro Fleming 2  
37100 Verona  
Italy

This person is:

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 applicant and inventor  
 inventor only (If this check-box is marked, do not fill in below.)

State (i.e. country) of nationality:  
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Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

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This person is:

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This person is applicant for the purposes of:  all designated States  all designated States except the United States of America  the United States of America only  the States indicated in the Supplemental Box

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 applicant and inventor  
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State (i.e. country) of residence:  
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This person is applicant for the purposes of:  all designated States  all designated States except the United States of America  the United States of America only  the States indicated in the Supplemental Box

Further applicants and/or (further) inventors are indicated on a continuation sheet.

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 inventor only (If this check-box is marked, do not fill in below.)

State (i.e. country) of nationality:

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Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

CICINSKI, Jan Josef  
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The University of Cambridge  
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This person Is:

applicant only  
 applicant and inventor  
 inventor only (If this check-box is marked, do not fill in below.)

State (i.e. country) of nationality:

GB

State (i.e. country) of residence:

GB

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Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

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GB

This person Is:

applicant only  
 applicant and inventor  
 inventor only (If this check-box is marked, do not fill in below.)

State (i.e. country) of nationality:

GB

State (i.e. country) of residence:

GB

This person is applicant for the purposes of:  all designated States  all designated States except the United States of America  the United States of America only  the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

WILLIAMS, Geoffrey Martyn  
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University Chemistry Laboratories  
The University of Cambridge  
Lensfield Road  
Cambridge, CB2 1EW  
GB

This person Is:

applicant only  
 applicant and inventor  
 inventor only (If this check-box is marked, do not fill in below.)

State (i.e. country) of nationality:

NZ

State (i.e. country) of residence:

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This person is applicant for the purposes of:  all designated States  all designated States except the United States of America  the United States of America only  the States indicated in the Supplemental Box

Further applicants and/or (further) inventors are indicated on a continuation sheet.

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Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

ZARAMELLA, Alessio  
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Via Alessandro Fleming 2  
37100 Verona  
Italy

This person Is:

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 applicant and inventor  
 inventor only (If this check-box is marked, do not fill in below.)

State (i.e. country) of nationality:

IT

State (i.e. country) of residence:

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This person is applicant for the purposes of:  all designated States  all designated States except the United States of America  the United States of America only  the States indicated in the Supplemental Box

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- NZ New Zealand.....
- PL Poland.....
- PT Portugal.....
- RO Romania
- RU Russian Federation.....
- SD Sudan
- SE Sweden
- SG Singapore
- SI Slovenia.....
- SK Slovakia.....
- SL Sierra Leone
- TJ Tajikistan.....
- TM Turkmenistan.....
- TR Turkey.....
- TT Trinidad and Tobago.....
- UA Ukraine.....
- UG Uganda.....
- US United States of America.....
- UZ Uzbekistan.....
- VN Viet Nam.....
- YU Yugoslavia.....
- ZA South Africa
- ZW Zimbabwe

Check-boxes reserved for designating States which have become party to the PCT after issuance of this sheet.

- CR Costa Rica.....
- DM Dominica.....
- TZ Tanzania.....

**Precautionary Designation Statement:** In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (*Confirmation of a designation consists of the filing of a notice specifying that designation and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit.*)

<b>Box No. VI PRIORITY CLAIM</b>		<input type="checkbox"/> Further priority claims are indicated in the Supplemental Box Where earlier application is		
Filing Date of Earlier Application (day/month/year)	Number Of earlier application	national application: country	regional application: regional Office	International application: receiving Office
item (1) (05.10.98) 05 October 1998	9821655.9	GB		
item (2)				
item (3)				
<input type="checkbox"/> The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) ( <i>only if the earlier application was filed with the Office which for the purposes of the present international application is the receiving Office</i> ) identified above as item(s): _____ <i>* Where the earlier application is an ARIPO application, it is mandatory to indicate in the Supplemental Box at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed (Rue 4.10(b)(ii)). See Supplemental Box.</i>				

**Box No. VII INTERNATIONAL SEARCHING AUTHORITY**

Choice of International Searching Authority (ISA) <i>(if two or more International Searching Authorities are competent to carry out the international search, indicate the authority chosen; the two-letter code may be used):</i> ISA/	Request to use results of earlier search; reference to that search ( <i>if an earlier search has been carried out by or requested from the International Searching Authority</i> ): Date (day/month/year)      Number      Country (or regional office)
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**Box. VIII CHECK LIST; LANGUAGE OF FILING**

This international application contains the following number of sheets:	This international application is accompanied by the item(s) marked below:
request : 6 description (excluding sequence listing part) : 82 claims : 8 abstract : 1 drawings : 14 sequence listing part of description : Total number of sheets : 111	1. <input checked="" type="checkbox"/> fee calculation sheet 2. <input type="checkbox"/> separate signed power of attorney 3. <input type="checkbox"/> copy of general power of attorney; reference number, if any: 4. <input type="checkbox"/> statement explaining lack of signature 5. <input type="checkbox"/> priority document(s) identified in Box No. VI as item(s): 6. <input type="checkbox"/> translation of international application into (language): 7. <input type="checkbox"/> separate indications concerning deposited microorganism or other biological material 8. <input type="checkbox"/> nucleotide and/or amino acid sequence listing in computer readable form 9. <input type="checkbox"/> other (specify): _____

Figure of the drawings which should accompany the abstract:	Language of filing of the International application: English
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**Box No. IX SIGNATURE OF APPLICANT OR AGENT**

*Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).*

Helen K. QUILLIN  
Agent for the Applicants

For receiving Office use only	
1. Date of actual receipt of the purported international application 2. Drawings <input type="checkbox"/> received: <input type="checkbox"/> not received:	
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application: 4. Date of timely receipt of the required corrections under PCT Article 11(2):	
5. International Searching Authority specified by the applicant: <b>ISA/</b>	6. <input type="checkbox"/> Transmittal of search copy delayed until search fee is paid

For International Bureau use only	
Date of receipt of the record copy by the International Bureau	

**PCT**  
**FEES CALCULATION SHEET**

For receiving Office use only

Annex to the Request

International application No.

Date stamp of the receiving Office

Applicant's or agent's  
file reference PG3565/PCT

Applicant Glaxo Group Limited et al

**CALCULATION OF PRESCRIBED FEES**

1. TRANSMITTAL FEE . . . . .

£55	T
£638	S

2. SEARCH FEE . . . . .

International Search to be carried out by \_\_\_\_\_

(If two or more International Searching Authorities are competent in relation to the international application, indicate the name of the Authority which is chosen to carry out the international search.)

3. INTERNATIONAL FEE

Basic Fee

The international application 111 sheets.

first 30 sheets . . . . .

£285	b <sub>1</sub>
£486	b <sub>2</sub>

remaining sheets additional amount

Add amounts entered at b<sub>1</sub> and b<sub>2</sub> and enter total at B . . . . .

£771	B
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**Designation Fees**

10 x 65 = £650

number of designation fees amount of designation fee payable (maximum 10)

Add amounts entered at B and D and enter total at I . . . . .

£1421	I
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(Applicants from certain States are entitled to a reduction of 75% of the international fee. Where the applicant is (or all applicants are) so entitled, the total to be entered as I is 25% of the sum of the amounts entered at B and D.)

4. FEE FOR PRIORITY DOCUMENT . . . . .

P
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5. TOTAL FEES PAYABLE

£2114

**TOTAL**

Add amounts entered at T, S, I and P, and enter total in the TOTAL box

The designation fee is not paid at this time

**MODE OF PAYMENT**

authorization to charge  
deposit account (see below)  
 cheque  
 postal money order

bank draft  
 cash  
 revenue stamps

coupons  
 other (specify) \_\_\_\_\_

**Deposit Account Authorization (this mode of payment may not be available at all receiving Offices)**

The RO/  is hereby authorized to charge the total fees indicated above to my deposit account.

is hereby authorized to charge any deficiency or credit any overpayment in the total fees indicated above to my deposit account.

is hereby authorized to charge the fee for preparation and transmittal of the priority document to the International Bureau of WIPO to my deposit account.

D01030

5 October 1999

Deposit Account Number

Date (day/month/year)

*Helen K. Quillin*  
Signature Helen K. QUILLIN  
Agent for the Applicants